

The opinion in support of the decision being entered today was not written for publication and is not binding precedent of the Board.

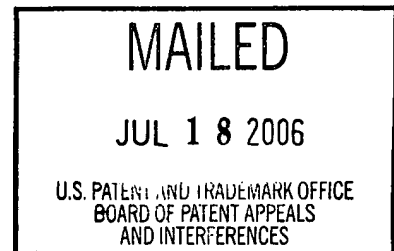
UNITED STATES PATENT AND TRADEMARK OFFICE

**BEFORE THE BOARD OF PATENT APPEALS
AND INTERFERENCES**

Ex parte DOUGLAS J. GOETZ, and MOHAMMAD F. KIANI

Appeal No. 2006-0292
Application No. 09/975,899

ON BRIEF



Before ADAMS, GREEN, and LEOVITZ, Administrative Patent Judges.

GREEN, Administrative Patent Judge.

DECISION ON APPEAL

This is a decision on appeal under 35 U.S.C. § 134 from the examiner's final rejection of claim 6, the only pending claim, which reads as follows:

6. A method of treating a cancer in an individual in need of such treatment, comprising the steps of:

irradiating a cancerous target tissue or organ in said individual;
and

administering to said individual a particle of biodegradable polymers or PEGylated copolymers comprising antibodies or antibody fragments that bind to ICAM-1 expressed on an endothelial cell of said irradiated tissue or organ and a pharmaceutical.

The examiner relies upon the following references:

Hallahan (Hallahan I) 6,159,443 Dec. 12, 2000

Hallahan (Hallahan II) WO 98/53852 Dec. 3, 1998

Patel et al. (Patel), "Spatially controlled cell engineering on biodegradable polymer surfaces," FASEB Journal, Vol. 12, pp. 1447-1454 (1998)

Mastrobattista et al. (Mastrobattista), "Cellular uptake of liposomes targeted to intercellular adhesion molecule-1 (ICAM-1) on bronchial epithelial cells," Biochimica et Biophysica Acta, Vol. 1419, pp. 353-363 (1999)

Claim 6 stands rejected under 35 U.S.C. § 103(a) as being obvious over the combination of Hallahan I, Hallahan II, the admission of prior art disclosed in the specification, Mastrobattista and Patel. After careful review of the record and consideration of the issue before us, we reverse.

DISCUSSION

Hallahan I is relied upon for teaching "a method of treating cancer, the method comprising the steps of exposing a target tissue or organ to the ionizing radiation and administering P-selectin antibody labeled delivery vehicle that carry active agent to the tumors." Examiner's Answer, page 3. The reference is also relied upon for teaching that following irradiation P-selectin is translocated to the cell membrane, which is complete thirty minutes after irradiation. See id. According to the examiner, "[t]he claimed invention differs from the reference teaching in that [Hallahan I] does not teach a particle of biodegradable polymers or PEGylated copolymers comprising antibodies that binds [sic, bind] to ICAM-1." Id. at 4.

Hallahan II is relied upon for teaching that exposing tissue to irradiation causes an increase in expression of several cell adhesion molecules, including ICAM-1. See id. Hallahan II, according to the examiner, “teaches the invention requires the over expression [of, sic] cell adhesion molecules, for example P-selectin or ICAM-1, in endothelial cells caused by ionizing radiation, which then allows said cell adhesion molecules to be targeted using specific binding composition and selected agents.” Id.

The examiner relies on the specification for teaching that it is known that exposure of normal and diseased tissue to irradiation causes an increase leukocyte infiltration, and also teaches that the key component of this process is the adhesion of leukocytes to the microvascular endothelium. See id. The examiner further notes that the specification teaches that “[i]n response to biochemical stimuli the endothelium become activated and increases its expression of receptors of several cellular adhesion molecule[s] [sic] including E-selectin, P-selectin and ICAM-1.” Id.

Mastrobattista is relied upon for teaching that antibodies bound to a biomolecular carrier may be used to deliver a pharmaceutical to sites where ICAM-1 expression is increased. See id. at 5.

Finally, Patel is relied upon for teaching drug carriers comprising a biodegradable polymer or a PEGylated copolymer, which provide the advantage of remaining in circulation for longer periods of time. See id.

According to the examiner, both the prior art and the claimed invention administer the same treatment, that is, irradiating a cancerous target tissue, and administering a biodegradable particle comprising an antibody that binds to a cellular adhesion molecule whose expression is increased by the irradiation, to achieve the same result, i.e., the treatment of the cancer. See id. The examiner thus concludes that

it would have been obvious to a person of ordinary skill in the art at the time the invention was made to apply the teachings of [Hallahan II], Mastrobattista [], Patel [], and Appellant's admissions of prior art set forth in the specification . . . to those of [Hallahan I] and substitute biomolecular carrier bearing antibodies to one species of cellular adhesion molecule i.e. P-selectin to another type of biodegradable polymers or PEGylated copolymers carrier bearing antibodies to another species of cellular adhesion molecule i.e. ICAM-1. The expression of any one of said adhesion molecules would be enhanced in target tissues after irradiation, as taught by [Hallahan II] and the known prior art disclosed in the Specification. . . .

One of ordinary skill in the art at the time the invention was made would have been motivated to do so, because it has been known for over 15 years that exposure of normal and diseased tissue to irradiation causes an increase[d] [sic] leukocyte infiltration and that the key component of this process is the adhesion of leukocytes to the microvascular endothelium, as taught by the known fact disclosed in the specification . . . and exposure [of, sic] tissue to irradiation causes an increase in expression of several species of cell adhesion molecules including ELAM-1, E-selectin and ICAM-1, in endothelial cells, as taught by [Hallahan II] and P-selectin labeled delivery vehicle was used to deliver[] [sic] drugs to target cancer tissue or organ where the expression of this cell adhesion molecule was increased by exposure [sic] said tissue or organ to irradiation, as taught by [Hallahan I] and biomolecular carrier, bearing antibodies to another cell adhesion molecule ICAM-1 effectively used to deliver[] [sic] drugs to the sites where the expression of ICAM-1 is increase[d] [sic], as taught by Mastrobattista [].

Id. at 5-6.

The burden is on the examiner to set forth a prima facie case of obviousness. See In re Fine, 837 F.2d 1071, 1074, 5 USPQ2d 1596, 1598-99 (Fed. Cir. 1988). “A rejection based on section 103 clearly must rest on a factual basis, and these facts must be interpreted without hindsight reconstruction of the invention from the prior art. In making this evaluation, all facts must be considered. The Patent Office has the initial duty of supplying the factual basis for its rejection. It may not, because it may doubt that the invention is patentable, resort to speculation, unfounded assumptions or hindsight reconstruction to supply deficiencies in its factual basis. To the extent the Patent Office rulings are so supported, there is no basis for resolving doubts against their correctness. Likewise, we may not resolve doubts in favor of the Patent Office determination when there are deficiencies in the record as to the necessary factual bases supporting its legal conclusion of obviousness.” In re Warner, 379 F.2d 1011, 1017, 154 USPQ 173, 178 (CCPA 1967), cert. denied, 389 U.S. 1057 (1968) (emphasis in original).

Appellants argue that the examiner has not set forth a prima facie case of obviousness, contending that the references as combined do not teach in vivo targeting of ICAM-1 expressed on the surface of endothelial cells. See Appeal Brief, page 8. According to appellants, the Hallahan references teach that P-selectin is localized to the vascular lumen and not on the vascular endothelial cell surface in irradiated tissue. See id. Moreover, appellants assert, Mastrobattista does not remedy the deficiency of the Hallahan references as

Mastrobattista merely teaches the use of anti-ICAM-1 immunoliposomes to target bronchial epithelial cells in vitro. See id. at 9. We agree that the examiner has not set forth a prima facie case of obviousness, and the rejection is reversed.

Hallahan II is relied upon by the examiner for its teaching that irradiation causes the expression of cell adhesion molecules (CAMs), such as ICAM-1 and P-selectin in endothelial cells. Reviewing the teachings of the Hallahan II reference, Hallahan II teaches that in using a CAM-based therapy to induce the expression of a CAM within a tumor, the CAM should meet the requirements of being readily inducible, having no basal cell surface expression in unirradiated tissue, and being inducible by radiation. See id. at 15. With respect to P-selectin, Hallahan II teaches that, upon exposure to ionizing radiation, it is translocated from WPBs (Weibel Palade organelles) to the blood-tissue interface of the endothelium, i.e., the lumen of the vasculature. See id. at 3-5. P selectin is constitutively expressed in WPBs, from where it moves to the vascular lumen within 30 minutes of irradiation, but is not detected in the pulmonary endothelium at 6 hours after irradiation. See id. at 16. The radiation dose required for increased P-selectin expression within the pulmonary vascular endothelium is 2-Gy, and thus the inventors concluded that P-selectin is a viable target for tumor-directed therapy. See id. at 16. Thus, in the Summary of the Invention, the inventors state that the invention is drawn to methods for delivering an agent to the vasculature of a subject comprising inducing P-

selectin translocation to the lumen of vascular endothelial cells through the use of ionizing radiation and administering a P-selectin targeting component. See id. at 6-7.

With respect to ICAM-1, Hallahan II teaches that it is not expressed at x-ray doses below 5 Gy, but shows an increase at 24 hours when higher x-ray doses were used; thus ICAM-1 induction requires high radiation doses, while expression is more prolonged. See id. at 16. ICAM-1 is expressed in the pulmonary capillary endothelium, and minimally within the endothelium of larger vessels. See id. As compared to P-selectin which has low constitutive expression, ICAM-1 has higher constitutive expression. See id. at 55. In addition, P-selectin was expressed in the endothelium of larger vessels, and not in the microvasculature. See id. at 67.

Because of the differences taught by Hallahan II in the induction of P-selectin versus the induction of ICAM-1 following ionizing radiation, we find that Hallahan II does not provide a teaching or suggestion of replacing antibodies to ICAM-1 for the antibodies to P-selectin in the methods disclosed by Hallahan I and Hallahan II for selectively delivering therapeutic agents to tumor vasculature. As discussed above, ICAM-1 is distinguishable from P-selectin by having a higher level of basal expression, a different vascular localization, and by requiring a higher level of ionizing radiation for induction. Thus, ICAM-1 does not meet the criteria that led Hallahan II to select P-selectin as a CAM that is useful in methods of targeting.

Even if we were to find that Hallahan II suggests the use of antibodies to ICAM-1 in the therapeutic methods using antibodies to P-selectin taught by Hallahan I and Hallahan II, at most the rejection rises to the level of obvious to try, and the references as combined provide no reasonable expectation of success of arriving at the claimed method. We find that there is no reasonable expectation of success because of the differences in the induction of P-selectin and ICAM-1 in response to exposure to ionizing radiation, as already discussed above. See The Gillette Co. v. S.C. Johnson & Son, Inc., 910 F.2d 720, 725, 16 USPQ2d 1923, 1928 (Fed. Cir. 1990) (“‘[o]bvious to try’ is not to be equated with obviousness under 35 U.S.C. § 103”).

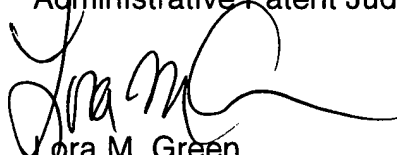
CONCLUSION

Because we conclude that the references as combined do not provide a prima facie case of obviousness under 35 U.S.C. § 103(a), the rejection of claim 6, the only claim on appeal, is reversed.

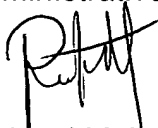
REVERSED



Donald E. Adams
Administrative Patent Judge



Lora M. Green
Administrative Patent Judge



Richard M. Lebovitz
Administrative Patent Judge

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